UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,805	02/12/2004	Scott L. Diamond	53893-5043	5374

23973 7590 04/30/2007

DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	**PAPER NUMBER**
1635	

MAIL DATE	DELIVERY MODE
04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,805	DIAMOND ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *1-18,22-26,30-52,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21,27-29,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2/16/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 2/27/07. Applicant's election with traverse of group 3 is acknowledged. The traversal is on the ground(s) that the invention was mischaracterized and MPEP 806.05(f) was misapplied. This is unpersuasive.

To support the argument that the invention was mischaracterized, Applicant asserts that the polyamide/steroid linkage disclosed in US 5,650,096 is counterintuitive to that of the instant compound. This is irrelevant because US 5,650,096 was not relied upon to demonstrate any particular mode of linkage. Instead it was relied upon as evidence that it is routine in the art to combine a lipid with a steroid that has been conjugated to a polyamine.

Regarding the nature of the conjugation, Applicant argues that the Examiner has not met the requirements of MPEP 806.05(f) or 803 because no evidence was produced to support the assertion that the polyamine and steroid elements need not be combined prior to mixing either the steroid or polyamine with a lipid. This is unpersuasive. It appears that Applicant misunderstood the Examiner's argument. The Examiner stated that in order to make the vehicle of invention 3, one need not follow the steps set forth in invention 1, wherein the steroid, conjugating reagent, and polyamine are all mixed together. One could instead mix together a steroid and a conjugating agent, purify the products from the reactants, and then mix the steroid-conjugating agent conjugate with the polyamine to produce a steroid-polyamine conjugate. This differs from mixing all three reactants together.

Regarding Applicant's requirement for evidence, MPEP 803 states "[e]xaminers must provide reasons and/or examples to support conclusions, but need not cite documents to support the restriction requirement in most cases." There is no need for evidence when reasoning is presented, so Applicant's arguments are unpersuasive. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-18, 22-26, 30-52, 54, and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/27/07.

Claims 19-21, 27-29, 52, and 53 are under consideration to the extent that the read on the elected invention of a cationic nonviral delivery vehicle, made by mixing together a steroid, or modification or derivative thereof, a conjugating agent, and a polyamine, wherein the conjugating agent conjugates the polyamine to the steroid or modification or derivative thereof, purifying the conjugate, and mixing it with a lipid.

Claim Objections

Claims 20, 21, and 27 are objected to because they depend from withdrawn claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20, 21, 27-29, 52, and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20, 21, 27-29, 52, and 53 are indefinite in their recitation of "a modification or derivative thereof". The specification provides no standard for determining the scope of the genuses of modifications or derivatives, and one of skill in the art could not know the metes and bounds of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 20, 21, and 27 are product by process claims. Such claims are not limited to the manipulations of the recited steps, but only the structure implied by the recited steps. See MPEP 2113. Absent evidence to the contrary, the following references anticipate the claimed structures.

Claims 20, 21, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al US 5,650,096.

Harris taught compositions comprising spermidine cholesterol carbamate and one or more colipids. The compositions formulated typically in a pharmaceutically-acceptable carrier. See e.g. claim 2; column 3, lines 1-5; and column 9, lines 46-51. In these compositions, chloroform can be thought of as a conjugating agent that is first reacted with cholesterol to form cholesteryl chloroformate. This molecule is subsequently reacted with Di-CBz-spermidine to give Di-CBz-spermidine cholesteryl carbamate. Removal of the CBz blocking groups gives the final product. See Fig. 13. Thus Harris anticipates the claims.

Claims 20, 21, and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by Mahato (US 6,696,038).

Mahato taught a cationic lipopolymer made by reacting cholesteryl chloroformate with a cationic polyamine. In these compositions, chloroform can be thought of as a conjugating agent that is first reacted with cholesterol to form cholesteryl chloroformate. This molecule is subsequently reacted with the polyamine to form the final product. See e.g. Fig. 1. Pharmaceutically acceptable carriers are disclosed at column 6, lines 46-50. The cationic lipid is formulated with a helper lipid. See column 4, lines 14-17. Thus Mahato anticipates the claims.

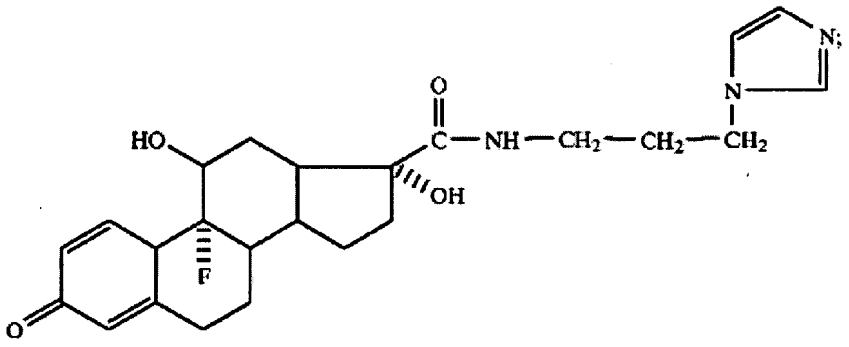
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

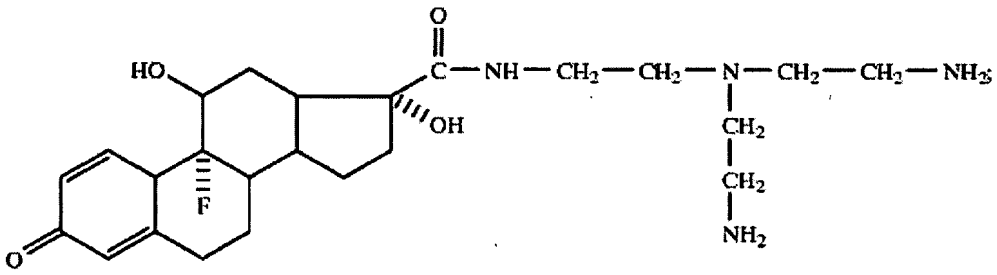
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20, 21, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolff et al (US 5,965,434).

Wolff taught amphipathic lipid compounds comprising a cationic, pH-sensitive, hydrophilic moiety for use in vesicular delivery systems for biologically active compounds such as nucleic acids. See title, abstract, and claims 8-14. The lipid portion could be a sterol or steroid, such as dexamethasone. The cationic portion comprises a primary, secondary, or tertiary amine. The cationic portion is joined to the lipid by a linker. See column 5, lines 1-16, claim 13, and dexamethasone derivatives at column 12, reproduced below.



Dexamethasone Derivative



Dexamethasone Derivative

Wolff does not explicitly disclose the combination of either of the dexamethasone derivatives with a colipid. However, it is clear that Wolff envisions formation of vesicles comprising a colipid such as phosphatidyl ethanolamine or dioleoylphosphatidyl ethanolamine (DOPE). See e.g. column 13, lines 41-44, column 14, lines 21-28 and 38-49, column 16, lines 36-40, column 38, lines 18-27, and column 39, lines 1-6. Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the lipid of Wolff with a colipid.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al (US 5,965,434) as applied to claims 20, 21, and 27 above, and further in view of Chaudhary et al (US 5,614,503).

Wolff taught amphipathic lipid compounds comprising a cationic, pH-sensitive, hydrophilic moiety for use in vesicular delivery systems for biologically active compounds such as nucleic acids. See title, abstract, and claims 8-14. The lipid portion could be a sterol or steroid, such as dexamethasone. The cationic portion comprises a primary, secondary, or tertiary amine. See above.

Wolff did not teach a lipid comprising dexamethasone conjugated to spermidine.

Chaudhary taught cationic lipids for nucleic acid delivery, comprising a lipid tail (such as a steroid) conjugated to a polyamine such as spermine. See e.g. Fig. 1 which exemplifies spermine-cholesterol. Chaudhary did not teach dexamethasone as a lipid moiety.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use spermine as a in the invention of Wolff, or to use dexamethasone in the invention of Chaudhary. It would have been clear to one of ordinary skill that it was routine to conjugate polyamines to lipids to make cationic lipids for nucleic acid delivery, and that both cholesterol and dexamethasone were used as lipids for this purpose. Furthermore, it was clear that spermidine was useful as a cationic head group. Both Chaudhary and Wolff taught chemistry for linking primary amines to steroids such that one of ordinary skill would have had a reasonable expectation of success in making the dexamethasone-spermine.

Claims 27, 28, 29, 52, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Harris et al (US 5,650,096), or Mahato (US 6,696,038), or Wolff et al (US 5,965,434), when any one of these references is combined with Lin et al (US 6,517,828).

Harris taught compositions comprising spermidine cholesterol carbamate and one or more colipids. The compositions formulated typically in a pharmaceutically-acceptable carrier. See e.g. claim 2; column 3, lines 1-5; and column 9, lines 46-51. In these compositions, chloroform can be thought of as a conjugating agent that is first reacted with cholesterol to form cholesteryl chloroformate. This molecule is subsequently reacted with Di-CBz-spermidine to give Di-Cbz-spermidine cholesteryl carbamate. Removal of the Cbz blocking groups gives the final product. See Fig. 13. Harris taught that the lipid compositions could be injected into a subject. See column 9, lines 58-64.

Mahato '038 taught a cationic lipopolymer made by reacting cholesteryl chloroformate with a cationic polyamine. In these compositions, chloroform can be thought of as a conjugating agent that is first reacted with cholesterol to form cholesteryl chloroformate. This molecule is subsequently reacted with the polyamine to form the final product. See e.g. Fig. 1. Pharmaceutically acceptable carriers are disclosed at column 6, lines 46-50. Mahato '038 also taught that the lipid compositions could be injected into a subject. See column 4, lines 4-17.

Wolff taught amphipathic lipid compounds comprising a cationic, pH-sensitive, hydrophilic moiety for use in vesicular delivery systems for biologically active compounds. See title and abstract. The lipid portion could be a sterol or steroid, such as dexamethasone. The cationic portion comprises a primary, secondary, or tertiary amine. The cationic portion is joined to the lipid by a linker. See column 5, lines 1-16, claim 13, and dexamethasone derivatives at column 12. Wolff also taught that the lipid compositions could be injected into a subject. See column 18, lines 5-10.

None of Harris, Mahato '611, Mahato '038, or Wolff taught a kit comprising a cationic lipid delivery vehicle, a compound, an applicator, and instructional material. However, each of these primary references taught a cationic lipid delivery vehicle and a nucleic acid compound for delivery, and the disclosure of each patent amounts to instructions for use.

It would have been obvious to one of ordinary skill in the art at the time of the invention to organize the elements of the invention of any of Harris, Mahato '611, Mahato '038, or Wolff into a kit because one of skill in the art appreciates that organizing experimental reagents and instructions prior to use is standard laboratory practice which reduces the frequency of errors. However, these references do not explicitly teach an applicator, even though each suggests injection or local delivery in vivo.

Lin taught methods of delivering lipid/nucleic acid complexes in vivo by injection. Lin used a syringe or needles injection device to perform injection. See column 47, lines 6-17.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use an injection device of Lin to perform the injections and local administration envisioned by any of Harris, Mahato '611, Mahato '038, Wolff in view of the teachings of Lin. One would have been motivated to do so because these devices are appropriate for administration of lipid/nucleic acid complexes in view of the teachings of Lin. It would have been similarly obvious to include an injection device in a kit comprising the elements of the invention of any of Harris, Mahato '611, Mahato '038, or Wolff because one of skill in the art appreciates that organizing experimental reagents, tools, and instructions prior to use is standard laboratory practice which reduces the frequency of errors.

Thus the invention as a whole was prima facie obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central

fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635